both satellites at the times of Jupiter's opposition in 1914 and 1915 and of the Ninth Satellite in 1916. The corresponding directions of the earth are shown by the arrows, and the relative positions of the earth and the two satellites explain how in 1914 the new satellite was found on the same plate as the Eighth. The orbits of the Sixth and Seventh Satellites, which are also shown in the figure, are drawn to scale but have not been projected into the plane of the figure.

The perturbations produced by the sun are very large for both satellites on account of their great distance from the primary. The orbits, therefore, are not even approximate ellipses; their points of greatest and least distance from Jupiter are indicated. It is of course impossible from the data now available to say much about the mean elements of the Ninth Satellite, but the mean period is likely not far from 745 days. The eccentricity appears to be a little less than that of the Eighth Satellite.

The magnitude of the Ninth Satellite was found by Mr. Shapley to be 18.3 on October 18 and 19, 1916,[3] which corresponds to 18.6 at mean opposition. With reasonable assumptions for the albedo and color index, this would indicate a diameter of about 15 miles. As seen from Jupiter the satellite at full phase would be between the 11th and 12th magnitudes, depending on its distance from the planet.

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AORTIC CELL CLUSTERS IN VERTEBRATE EMBRYOS

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Aortic cell clusters in mammals were first described by Maximow[1] (p. 517) in rabbit embryos. Minot[2] (p. 523) subsequently described similar structures in human embryos of from 8 to 10 mm. length and in rabbit embryos. Emmel[3] reported aortic cell clusters in rat embryos, rabbit embryos, and in pig embryos of from 6 to 15 mm. Jordan[4] discovered these clusters in pig embryos (10 to 12 mm.) at about this same time, and reported their presence also in mongoose and turtle embryos. Emmel[5] later published a detailed description of the aortic clusters of the pig embryo. Meanwhile I had observed them also in chick embryos of 3 to 4 days' incubation. Dantschakoff[6]

had already reported similar structures in the chick. Aortic cell clusters would seem to be a common feature of certain early stages of vertebrate development.

All of the above-named investigators agree in interpreting the constituent cells of the clusters as hemoblasts, variously designated as 'lymphocytes,' 'mesameboids,' progenitors of macrophages ? hemoblasts. Minot[2] alone disagrees with the otherwise unanimous conclusion that they represent endothelial differentiation products. That they are endothelial derivatives, however, rather than accretion products of hemoblasts from the circulating embryonic blood is easy of demonstration. Aortic cell clusters represent one phase of the general hemogenic capacity of embryonic endothelium.

The doctrine of the partial endothelial origin of hemoblasts from embryonic endothelium has become associated with the monophyletic hypothesis of blood cell origin (Maximow)[1] that of the non-hemogenic capacity of endothelium with the polyphyletic and diphyletic hypotheses (Stockard).[7] The question of the genetic relationship between endothelium and certain cellular elements of the embryonic blood touches also the 'angioblast' theory of His. The two chief tenets of this theory are : (1) the inability of intraembryonic mesenchyme to produce blood vascular tissue, and (2) the incapacity of endothelium to differentiate into blood cells. Abandonment of the first tenet has been forced largely through the experimental work of Hahn,[8] of Miller and McWhorter,[9] of Reagan,[10] and of Stockard;[7] and the morphologic studies of Schulte[11] on the cat embryo, those of McClure[12] on the trout embryo, and the studies of Huntington[13] on the development of the lymphatics in amniotes. The surrender of this portion of the original theory is gradually being made by some of its staunchest advocates (vide Sabin[14]). The disproof of the second tenet is the chief burden of this investigation.

The material studied includes three mongoose embryos of 5, 6, and 7 mm. respectively, a series of pig embryos of from 8 to 12 mm., chick embryos of the third and fourth day of incubation, and a series of twenty loggerhead turtle embryos ranging from the second to the thirty-second day of incubation.[15] These embryos are variously preserved and stained, the several methods including fixation with Helly's fluid and staining with Giemsa's solution.

This description confines itself almost exclusively to the 5 mm. mongoose embryo and the 12 day turtle embryo. This selected material is at just the proper stage of development to furnish the key for the correct interpretation of the larger aortic clusters of the 10 mm. pig embryos.

The study was approached by way of the yolk sac of the mongoose embryo. The endothelial origin of hemoblasts can here be readily demonstrated. These observations on the mongoose yolk-sac confirm my[16] previous findings regarding the hemogenic rôle of yolk-sac endothelium in the 10 mm. pig embryo.

The second step involved a search for similar intraembryonic phenomena. It seemed reasonable to expect that, since the yolk-sac mesenchyme could differentiate directly into blood cells and into endothelium, and since the endothelium could subsequently transform into blood cells then the same order of events should probably follow also in the intraembryonic mesenchyme; and further, since mesenchyme is the fundamental hemogenic tissue, and since both endothelium and mesothelium in the embryo are only slightly modified mesenchyme (chiefly by means of the mechanical factor of pressure—vide Huntington,[13] p. 265), then embryonic mesothelium and endothelium should both in the only slightly differentiated condition be capable of producing cellular blood elements (hemoblasts).

That mesothelium can differentiate into vascular tissue has been shown by Bremer[17] in the case of the body stalk of a 1 mm. human embryo. Examination of the intraembryonic endothelium in the pig and mongoose revealed, in the smaller pericerebral blood channels, an occasional endothelial cell rounding up and taking on hemoblast features and finally separating from the endothelial wall; and led to the discovery and detailed study of the aortic clusters of hemoblasts, with the origin and significance of which this paper is largely concerned. Moreover, investigation of the pericardial mesothelium disclosed very similar clusters, both attached to the visceral and the parietal pericardium, and lying free within the pericardial cavity. Emmel[18] has recently described comparable structures in the 12 mm. pig embryo. Occasional individual cells can also be seen in process of separation from the visceral pericardium in the mongoose embryo.

The suggestion has been made that what is interpreted as a hemoblast in the act of differentiation and separation from the endothelium, is simply an endothelial cell in preparation for division. Many dividing endothelial cells from the pericerebral mesenchyme were observed with this suggestion in mind. But no endothelial cell, even at metaphase of mitosis, appeared rounded up in the same fashion as the differentiating hemoblast, nor to the same degree; at most it was merely a stout fusiform body, without the distinct unilateral bulge equatorially which is characteristic of the hemoblast during the later stages of its separation from the endothelium. Moreover, the nucleus of even the

stoutest endothelial hemoblast at this stage is in the typical resting condition.

As regards the aortic cell clusters, the 5 mm. mongoose embryo shows admirably various early stages in their origin and development, and so furnishes the key to the interpretation of the later products. And the 12 day loggerhead turtle embryo shows besides, the peculiar intravascular encapsulated cell clusters, and the endothelial strands, recently noted also for a 12 mm. pig embryo by Emmel[5] in a footnote to his paper (p. 407) on aortic cell clusters in mammals; and the conditions in this respect also are such as appear to solve the mystery of their genetic significance.

The aortic cell clusters in the mongoose embryo of from 5 to 7 mm. range from such as are composed of only a single cell to those composed of a score or more. Single cells or groups of two or three can be seen separating from the endothelium at any point, even along the mid-dorsal line. Larger groups are found only in the ventral and ventro-lateral portions, frequently in more or less close relation to the mouths of the lateral mesonephric branches or the ventral intestinal rami. This proliferative activity of the aortic endothelium is present only in the abdominal portion of the aorta, approximately coextensive with the mesonephroi. Single endothelial cells may round up and take on hemoblast features and separate from the wall in exactly the same manner as that by which the hemoblasts are derived from the endothelium of the yolk-sac vessels and in the pericerebral vascular channels. The process is the same in the yolk sac and the embryo, and indicates a common hemogenic capacity of embryonic endothelium.

The mongoose material shows also the initial stages in the formation of the larger cell clusters. Throughout the ventral half of the abdominal aorta, the endothelium at certain points appears to buckle into the lumen. This invaginated area may be more or less extensive, and may include a considerable portion or none of the subjacent mesenchyme. The cause of the buckling remains obscure, though the suggestion lies close to hand that it may be related to the caudal shifting of the embryonic representatives of the celiac, superior mesenteric and inferior mesenteric arteries; a process dependent in part at least upon the presence of a less rigid and less differentiated endothelium ventrally, permitting thus of an inequality of growth as between the ventral and dorsal walls or allowing for the formation of successively lower connecting vascular segments for the migrating definitive stems.

The endothelium seems to be lacking centrally underneath the cell clusters. This is explained by the fact that the larger clusters arise by

an invagination of the endothelium over an area of some extent rather than by process of proliferation of one or several differentiating endothelial cells. Proximally the clusters show transition stages between endothelial cells and hemoblasts (laterally) and between mesenchymal cells and hemoblasts (centrally). The subjacent mesenchyme of the larger clusters may become thickened, sometimes assuming the features of a stratified endothelium, and the nuclei are relatively much more abundant, smaller, and less differentiated. In the larger clusters, the peripheral cells, some of which show early erythroblast features, begin to separate from the central group. Within the clusters some of the cells are in mitosis, while the nuclei of others may appear at some phase of amitotic division; and an occasional cell may show phagocytic properties. Sometimes the core of the cluster shows transition stages between the endothelium or mesenchyme and hemoblasts. Many of the nuclei subjacent to the cluster appear at some phase of amitotic division. The absence of mitotic figures in the subjacent endothelium constituted the strongest of the three objections made by Minot[2] against the interpretation of the aortic clusters as endothelial derivatives. It would seem that the method of proliferation is here largely amitotic.

The aortic cell clusters of the mongoose embryo originate from the cells of an invaginated area of endothelium; they enlarge by intrinsic growth and differentiation, not by accretions from the circulating blood. Similar clusters appear also in the superior mesenteric artery. In a 10 mm. pig embryo a large aortic cluster, 130 microns in diameter, appears near the mouth of the superior mesenteric artery and consists of a hundred or more cells. Clusters appear also along the greater length of this definitive aortic stem.

In the 12 day loggerhead turtle embryo, encapsulated clusters and extensive strings of hemoblasts attached to the endothelium appear in the inferior vena cava, near the point of fusion of the original paired subcardinal veins; and in the jugular veins. The endothelial strands, some of the cells of which bear hemoblast features, are most probably only another aspect of the general hemogenic capacity of young endothelium. Emmel[5] saw similar strands in the proximal portion of the left umbilical artery, and in the aorta of this level, in two 12 mm. pig embryos, and suggests that they may be related to the fusion of the two original dorsal aortae. In the case of the development of the inferior vena cava, the coincident fusion between the originally separate post—and sub-cardinal veins involves the formation of young, less differentiated, endothelium and so offers a favorable site for hemoblast production by endothelium.

The encapsulated cluster present in this same region of the inferior vena cava may be explained as follows: Subjacent to such clusters the mesenchyma appears to be differentiating into hemoblasts; this observation may give the clue to the correct interpretation of these clusters. If the invaginating area of endothelium included a considerable portion of such differentiating (vascularising) mesenchyme, then the peripheral cells might possibly be so far outstripped in the expression of their hemogenic potentiality as to be forced, perhaps principally by reason of internal pressure from the differentiating and proliferating cells, to continue development along the line already begun, namely into definitive endothelium.

The whole series of phenomena above described seems to me to signify only various aspects of the same process, the hemogenic activity of embryonic endothelium. Though perhaps not essential, it appears nevertheless to be a normal process, consequent to the inherent capacity of endothelium to produce hemoblasts.

Emmel[5,18] interprets the endothelial and mesothelial desquamation products, both cells and clusters, in terms of the stimulative effect of a pathologic factor upon the endothelium; a toxin whose source is in the degenerating cells of atrophying redundant ventral aortic rami, and in degenerating erythrocytes in the serous cavities in the case of the mesothelia.

That atrophying vascular stems are present at this stage, both in relation to the aorta, and the inferior vena cava, cannot be disputed. In the 7 mm. mongoose embryo the solid regressive ventral aortic stems are especially conspicuous. At least a portion of the caudal shifting of the three large aortic rami is due to a progressive atrophy of upper portions of a connecting net of vessels. But coincident with this phase of a regressive development among the upper roots, there may possibly be a new formation of lower roots. I incline to see the cause of cluster formation in the latter possibility rather than in the former fact.

Great stress is laid by Emmel upon the structure of the atrophying rami. Some of these are occluded by intravascular collections of hemoblast-like cells, both in the 10 mm. pig embryo and in the 7 mm. mongoose embryo. With these intra-arterial cell masses some of the aortic clusters are intimately related. Emmel ascribes the presence of this intra-arterial mass to the stimulative action of a dilute toxin, presumably liberated by the regressive aortic branches. This explanation is suggested by an alleged comparable pathologic process where endothelium is believed by certain pathologists (e.g., Mallory[19]) to be stimulated to the formation of 'endothelial leukocytes' ('large mononuclear leuko-

cytes') by dilute toxins such as are produced by typhoid and tubercle bacilli. A more likely interpretation, it seems to me, would attribute the presence of the intra-arterial cell mass of the smaller rami to the relatively slightly differentiated character of the endothelium. The occlusion of the rami and the degeneration (karyorrhexis) of the cells would thus be a secondary effect of the constriction of the regressive atrophying vessels. In other words, the intra-arterial cell mass is not the *result* of the action of a toxin; but the occlusion and degeneration (and the possible formation of a 'toxic' substance) are all the related common sequalae of the shrinking of the atrophying vessel around a previously present, normally produced, mass of hemoblasts.

But the most damaging countervailing evidence to the interpretation of endothelial cell-cluster derivatives as the result of a stimulative toxin, consists in the fact that in the definitive superior mesenteric artery of the 10 mm. pig embryo numerous cell clusters appear, even in the middle third of the vessel which is a level that could not be directly affected by a possibly later further caudal migration of this artery through atrophy of its present connecting aortic root; and which shows not the slightest indication of atrophy or degeneration, either of the vessel wall or the included blood cells, other than the presence only of hemoblast clusters.

In all the forms studied (pig, mongoose, chick, turtle) the superior mesenteric artery also contains both clusters and individual cells in process of differentiation into hemoblasts. Moreover, not all the ventral rami which ultimately disappear contain clusters or intra-arterial cell masses; and occasional clusters are relatively far removed from the mouths of any aortic branches.

If some toxin were correctly held responsible for the endothelial activity in the formation of isolated and aggregated hemoblasts, it becomes very difficult to explain its localized effect. The same objection holds regarding the clusters in the superior mesenteric (vitelline) artery. If the source of the toxic substance is here supposed to be degenerating cells of the yolk sac, its influence should be felt far beyond this vessel itself, or the ventral portion of only the abdominal segment of the dorsal aorta. A certain amount of cell disintegration no doubt occurs over wide areas of embryonic vascularised tissue, and numerous primitive venous channels also disappear; but, though extensively studied by various investigators, no cell clusters have been reported except in the ventral portion of the dorsal aorta (and in this paper, in the inferior vena cava near the point of fusion of the subcardinal veins), levels where a less differentiated endothelium is present as well as re-

gressive vascular channels. Furthermore, no atrophy of vessels nor any uncommonly extensive disintegration of erythrocytes have appeared in the yolk sac at these early stages (7 mm. in mongoose embryo; 10 mm. pig embryo) and yet the endothelial derivation of hemoblasts is very active.

It may be emphasized that as regards the endothelial origin and the composition of the aortic cell clusters, and as regards the mesothelial origin of cellular elements of the serous fluids, Emmel and I are in essential agreement. But Emmel views these structures as the result of the presence of a stimulating toxin; I see in them only the expression of a normal inherent capacity of embryonic endothelium to produce blood cells. The explanation of the limited distribution of the clusters is to be found in a relationship to young or newly formed, only slightly differentiated, endothelium; rather than in a connection with regressive blood vessels and an associated toxic substance.

All the facts seem to fit better the hypothesis that the hemogenic activity of embryonic endothelium is a normal function at a certain stage of embryonic development, than that the causative stimulus is a toxin derived from degenerating vascular tissues.

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